

## Abstracts

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emergency department visits in 1999–2001 by individuals aged 25–64 with primary diagnosis of pneumonia, antibiotic prescription within three-days, chest x-ray on index date, continuous enrollment for 12-months prior, 30-days after index visit. Exclusion criteria: antibiotic prescription, pneumonia diagnosis, or hospitalization in prior 30-days; initial therapy with multiple antibiotics; in prior 12-months residence in a long-term care facility or diagnosis of cancer of bronchus or lung, secondary malignancy, HIV/AIDS, cystic fibrosis, immunity disorders. We considered the following comorbid illnesses: chronic liver, renal or lung disease; cerebrovascular disease; cardiac disease; diabetes mellitus; malignancy. **RESULTS:** A total of 5748 cases met criteria, 13.9% initially seen in the emergency department. Of these, 16.8% had one comorbidity, 3.5% had multiple comorbidities. Macrolides were the most common initial therapy (66.5%), followed by quinolones (17.9%). Quinolone use more than doubled from 1999 to 2001, from 11.8% to 24.3% in patients without comorbidity, from 12.1% to 33.8% in patients with comorbidities. Overall, 13.1% received a change in therapy without subsequent hospitalization, another 3.0% were hospitalized. Females were more likely to change therapy than males (15.9% vs. 10.5%,  $p < 0.0001$ ) but not more likely to be hospitalized (3.0% for both). Failure rates were strongly associated with number of comorbidities ( $p = 0.0004$ ), particularly in rates of subsequent hospitalization: 2.4% for no comorbidities, 4.9% for one comorbidity and 7.5% for multiple comorbidities. Hospitalization without secondary outpatient therapy was common: 13.5% for patients without comorbidity, 24.9% for one comorbidity, 28.6% for multiple comorbidities. **CONCLUSION:** While macrolides were the most common therapy, quinolone usage was substantial and rising rapidly regardless of comorbidity. Hospitalization for patients failing therapy was fairly common even in patients without comorbidity.

PIN2

#### **EFFECT OF INAPPROPRIATE ANTIBIOTIC THERAPY ON CLINICAL OUTCOMES OF PATIENTS WITH PSEUDOMONAS AERUGINOSA BACTEREMIA**

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**OBJECTIVE:** Infections due to *P. aeruginosa* are associated with increased likelihood of death and morbidity. Empiric therapy is often difficult due to increased resistance noted with this organism. The purpose of this study was to determine the impact of inappropriate initial empiric therapy on health outcomes of patients with *P. aeruginosa* bacteremia. **METHODS:** Retrospective cohort study of hospitalized patients with their first episode of *P. aeruginosa* bacteremia. Patients were stratified based on appropriateness of antipseudomonal therapy. Inappropriate initial empiric therapy was defined as receipt of antibiotic therapy to which the isolate displayed in vitro resistance. Data collected included discharge mortality, new ICU admit, new requirement for ventilator therapy or hemodialysis, and length of hospital stay. **RESULTS:** A total of 87 patients (71% males/29% females) aged  $58 \pm 17$  years (mean  $\pm$  SD) were identified between January, 2002 to April, 2004. Overall mortality was 44%. Forty-nine percent of patients received inappropriate antibiotic therapy. ApacheII score were significantly higher in patients that died ( $p = 0.003$ ). Mortality rates were significantly higher in patients treated with inappropriate empiric therapy (63%) compared to patients treated appropriately (39%, OR = 2.97,  $p = 0.024$ ). New requirements for ICU admission, hemodialysis, or ventilator did not differ between the two groups. **CONCLUSIONS:** Inappropriate initial empiric therapy

in patients with *P. aeruginosa* bacteremia significantly increased mortality rates.

PIN3

#### **DURATION OF ANTIBIOTIC TREATMENT IN HOSPITALIZED PATIENTS WITH COMPLICATED SKIN AND SKIN STRUCTURE INFECTIONS (cSSSI): FINDINGS FROM A CLINICAL STUDY COMPARING TIGECYCLINE AND VANCOMYCIN/AZTREONAM**

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**OBJECTIVES:** We sought to evaluate which risk factors may be implicated in prolonged duration of antibiotic treatment in hospitalized patients with complicated skin and structure infections (cSSSI). **METHODS:** We pooled data from two double-blind, randomized, multinational, clinical trials among patients with cSSSI. Patients were randomly assigned to receive either tigecycline (initial 100 mg dose, followed by 50 mg twice daily) or vancomycin with aztreonam (1g vancomycin plus 2g aztreonam, twice daily) via IV administration. Treatment termination was based on physician assessment of resolution of signs and symptoms of infection, with formal test of cure (TOC) at least 12-days later. We used a Cox proportional hazard (CPH) model to identify potential clinical risk factors for longer time-to-treatment termination. **RESULTS:** Among 1041 patients in the modified intent-to-treat (m-ITT) population with complete hospitalization data, deep/extensive cellulitis (59%) was the most common cSSSI diagnosis, spontaneous infection (51%) was the typical etiology, and diabetes (22%) was the most common comorbidity. No significant differences were observed in baseline characteristics. Median treatment duration was eight-days for each treatment group. The estimated CPH model identified diabetes ( $p < 0.0001$ ), female sex ( $p = 0.017$ ), infected ulcer ( $p = 0.001$ ), and use of concomitant antibiotics ( $p = 0.002$ ) as independent risk factors for significantly longer treatment duration. Adjusting for these risk factors, tigecycline was associated with a trend toward shorter treatment duration overall ( $p = 0.072$ ) and within the diabetes, infected ulcer, and female strata. There was no difference across the treatment groups in the rate of cure at the TOC visit ( $p = 0.197$ ). **CONCLUSIONS:** Diabetes, female sex, infected ulcers, and use of concomitant antibiotics emerged as significant risk factors for prolonged treatment duration in cSSSI. Tigecycline, the first in a new antibiotic class, the glycylcyclines, was associated with a trend toward shorter treatment duration, once the risk factors were adjusted for.

PIN4

#### **IMPACT OF EMPIRIC ANTIFUNGAL THERAPY ON MORTALITY IN HOSPITALIZED PATIENTS WITH BLOODSTREAM CANDIDEMIA**

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**OBJECTIVE:** The objective of this study was to determine the impact of empiric antifungal therapy on mortality in hospitalized, non-neutropenic patients with bloodstream candidemia. **METHODS:** Retrospective cohort study to evaluate the effect of empiric therapy on mortality in patients with bloodstream candidemia. Medical and hospitalization history were collected from the medical charts of patients hospitalized from 2002 to 2004 with their first documented episode of candidemia. Patients were grouped by APACHEII scores and choice of empiric antifungal therapy (narrow spectrum: fluconazole or itraconazole; broad spectrum: amphotericin, caspofungin, or voriconazole). Impact

of empiric antifungal therapy was assessed using univariate techniques and multivariate logistic regression. **RESULTS:** A total of 81 patients were evaluated in this study. Forty-four percent received broad spectrum, 46% received narrow spectrum, and 10% received no therapy. Overall mortality was 51%. APACHEII >20 and narrow spectrum empiric therapy were independent predictors of mortality ( $p = 0.011$ ). Mortality rates were similar in patients with Apache score >20 given broad (85%) or narrow spectrum (79%) empiric therapy. However, in patients with lower APACHEII scores (<20), mortality was significantly lower in patients started on broad spectrum (4%) compared to narrow spectrum (46%). After excluding patients who died while on therapy, average length of therapy was similar for both groups (11–12 days). **CONCLUSIONS:** Patients with candidemia with an APACHEII score <20 treated with broad spectrum antibiotics had lower mortality rates compared to those initially treated with narrow spectrum antifungal therapy.

#### PIN5

##### **COST ANALYSIS OF A FEBRILE NEUTROPENIA ALGORITHM WITH RESPECT TO EMPIRICAL ANTIFUNGAL THERAPY IN ADULT HEMATOLOGY/ONCOLOGY PATIENTS**

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**OBJECTIVE:** Neutropenia following cancer chemotherapy is a major risk factor for invasive fungal infections (IFIs). The high rates of mortality associated with IFIs warrants the use of empirical antifungal therapy. Conventional amphotericin B (CAB) is considered to be the standard of care in persistently febrile neutropenic patients; however, infusion-related reactions and nephrotoxicity limit its use. Although liposomal amphotericin B (LAmB) has demonstrated similar efficacy to CAB and is generally well tolerated, it is associated with a high acquisition cost. Voriconazole is a potential alternative for empirical therapy of IFIs. An algorithm for the management of febrile neutropenia (FN) was implemented at the University of Michigan Health System (UMHS). The new algorithm, implemented in January, 2003, recommends voriconazole as the preferred antifungal for adult Hematology/Oncology patients with FN, except those with evidence of hepatic dysfunction or who are receiving gemtuzumab. The objective of this study was to determine the financial impact of this algorithm. **METHODS:** Patients on the adult Hematology/Oncology service who first received either LAmB or voriconazole over a two-year period were identified retrospectively using the UMHS Data Warehouse. Costs were evaluated from the perspective of the Health System and compared between the voriconazole and LAmB groups from first the antifungal dose to the time of hospital discharge. **RESULTS:** Seventy-eight patients were included in the analysis (42 LAmB and 36 voriconazole). Antifungal cost per patient declined from \$4278 to \$3331 in the voriconazole group. This represented a decrease of \$947 per patient. Laboratory cost per patient increased by \$579. The total cost per patient initiated on voriconazole decreased by \$1502. **CONCLUSION:** The implementation of an algorithm incorporating voriconazole as the preferred antifungal agent for empiric treatment of febrile neutropenia was associated with decreased spending on antifungal agents, increased laboratory costs, and a decrease in total costs.

#### PIN6

##### **ECONOMIC EVALUATION OF VACCINATION AGAINST STREPTOCOCCUS PNEUMONIAE IN GERMANY INCLUDING HERD IMMUNITY EFFECTS**

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**OBJECTIVES:** Children vaccinated with Prevenar have been shown to be at reduced risk of meningitis, bacteraemia, pneumonia and acute otitis media. Vaccination may also affect risk in unvaccinated individuals by reducing the circulation of infectious organisms in the community, a phenomenon known as herd immunity. This analysis examined the economic consequences of Prevenar vaccination incorporating herd immunity effects. **METHODS:** An existing model was adapted to consider herd immunity effects in Germany. Vaccine coverage of 83% was assumed and the model estimated the number of pneumococcal events, deaths and associated costs in vaccinated individuals over ten years. Efficacy came from a large randomised study in the US, corrected for age specific German epidemiology. Changes in rates of infection with vaccine susceptible organisms have been found by the Active Bacterial Core Surveillance Network in the US, where Prevenar has been in use for several years. Costs were estimated from the perspective of society, including four vaccine doses, treating pneumococcal disease in hospital and the community, long term disability resulting from infections and social security payments. Future costs were discounted at 5%. **RESULTS:** The model estimated that vaccination would avoid 98 cases of meningitis, 376 cases of septicaemia and 19 deaths in vaccinated individuals. Using the percentage reduction in disease observed in the USA, the model estimated that a further 3940 deaths would be avoided annually in unvaccinated individuals, mostly by reducing the incidence of pneumonia in the elderly. The cost per life year gained was 43,000€ in the vaccinated cohort alone, but vaccination was cost saving when herd immunity effects were incorporated. Findings are sensitive to disease incidence, long-term costs of meningitis and vaccine cost. **CONCLUSION:** The model showed that the benefits of Prevenar extend beyond vaccinated individuals. Failing to consider herd immunity effects may substantially understate the economic benefits of vaccination.

#### PIN7

##### **AN UPDATED EVALUATION OF THE COST-EFFECTIVENESS OF VACCINATING ADOLESCENTS FOR PERTUSSIS**

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**OBJECTIVES:** Acellular pertussis vaccines make immunization of adolescents more feasible and may help reduce the burden of pertussis. Based on recent estimates indicating that infection may be much more common than previously thought, we updated an economic evaluation of adolescent pertussis vaccination to assess programs in this new context. **METHODS:** A model was previously developed to estimate the effects of pertussis vaccination of adolescents (ages 11–18) including herd immunity. Inputs for the US were taken from literature, government data and cost databases. Recently published incidence estimates replaced previous CDC-based ones. Where adequate data were unavailable, estimates were agreed to by an expert panel (the Global Pertussis Initiative). Health benefits were quantified as cases, deaths, and disability avoided, and life years gained. Both direct medical costs and lost productivity costs were considered. All outcomes were discounted at 3% per year. Time horizon was ten years. Extensive uni- and multivariate sensitivity analyses were completed. **RESULTS:** Adopting new incidence estimates dramatically improves the value of adolescent vaccination, with cases avoided exceeding two million over ten years. The economic results switch from the original cost-effective situation to direct medical savings of \$719 million and societal of \$1.2 billion, if parameters other than incidence are unchanged. Sensitivity analyses show that the cost per case would need to be < 10% of